REMARKS

Interview Statement:

Applicants appreciate the Examiner's courtesy in granting the personal interview of April 8, 2008 with the undersigned. The attendees further included Dr. Salim Shah (Reg. No. 60,866), Examiner Meah and Primary Examiner Prouty.

As a procedural matter, the Examiner confirmed that the Office Action is non-final and that claim 16 is allowed.

On substantive issues, the interview mainly focused on Rowbury et al. In the Examiner's view, Rowbury teaches that exogenous gene expression induces stress response, and that it is well known that stress in *E. coli* may be monitored by measuring hydrogen peroxide decomposition. In view of the above, the Examiner considered that it would have been obvious to select an *E. coli* strain which actively expresses the PAL gene simply by measuring its stress response.

Applicants' representative challenged the Examiner's assertion that Rowbury et al (or the prior art in general) teaches that stress response is correlated with expression of exogenous material. Applicants' representative also disagreed with the Examiner's assertion that reference to phage in Rowbury et al is such a teaching. In this regard, Applicants' representative drew the Examiner's attention to the phase "lethal biological agents" and distinguished exogenous PAL expression from *external* agents as indicated in the reference.

Applicants' representative, in turn, urged patentability pointing to [0046] of the Applicants' published application. Namely, it is counter-intuitive to select a strain which

actively expresses an exogenous gene based on stress response. This is because the stress response acts to suppress expression of the exogenous gene and therefore alleviates stress.

The Examiner and Primary Examiner did not find this argument persuasive, again reiterating that a high stress response (as monitored by hydrogen peroxide decomposition) is indicative of high expression activity (expression of an exogenous gene), and that it is natural to select a strain having high expression activity based on its stress response.

Applicants' representative further noted that stable expression of repeated sub-culturing is different from high activity expression. That is, even if it would have been obvious to select for high expression activity based on stress response, which Applicants would dispute, claim 7 (as now incorporated into claim 4) defines a strain that is separately patentable (no connection in the prior art between stress response and stable expression). The Examiner also did not find this argument to be persuasive, because, according to the Examiner, there is little difference between high expression activity (of an exogenous gene) and stable expression over a series of subcultures.

No agreement was reached.

Description of Claim Amendments:

Claim 4 has been amended to incorporate therein the recitation of claims 6 and 7, to recite that the phenylalanine ammonia lyase gene is a gene whose expression tends to decrease by causes other than loss or mutation of the plasmid when introduced into an *E. coli* other than the claimed strain, and that the initial amount of the phenylalanine ammonia lyase gene expression is maintained or enhanced during subculture. Claims 6 and 7 have been canceled.

Withdrawn claim 1 directed to a method for selecting an *E. coli* has been amended to include all of the limitations of amended claim 4. If claim 4 is found to be allowable, Applicants respectfully request rejoinder of method claim 1 pursuant to MPEP § 821.04. Claims 2 and 3 corresponding to the limitations of claims 6 and 7 have been canceled.

Additionally, claims 17-19 directed to a non-elected invention have been canceled. Applicants reserve the right to file a divisional application directed to the canceled subject matter.

Review and reconsideration on the merits are requested.

Response to Prior Art Rejection:

Claims 4, 6-7, 10-13 were rejected under 35 U.S.C. 103(a) as obvious over Rowbury et al. in view of Lockwood et al. (WO 94/19472) and Seaver et al. The Examiner alleged that Rowbury et al. teach that in cells of microorganisms, such as *E. coli,* the stress response increases upon expression of exogenous material including genes. The Examiner further alleged that it would be obvious to one of ordinary skill in the art to express an *E. coli* strain with an exogenous PAL gene, as taught by Lockwood, and to use Seaver's method of measuring hydrogen peroxide decomposition activity to select said *E. coli* strain based on stress response.

Applicants traverse, and respectfully request the Examiner to reconsider in view of the amendments to the claims and the following remarks.

Rowbury et al. teach that **lethal biological agents** such as antibiotics, colicins, and bacteriophages induce stress response. By definition, all the listed agents kill bacteria. There is no indication in the reference that the transformed exogenous gene is a lethal biological agent. Furthermore, the reference does not teach whether exogenous gene expression actually induces

stress response. In fact, it is well known in the art that the stress response is a defense mechanism and it acts against exogenous material when introduced into a cell. Thus, it would be counter-intuitive to observe a positive correlation between stress response and exogenous gene expression. This aspect of Applicants' invention is described in the paragraph bridging pages 11-12 of the specification (i.e., paragraph [0046] of Applicants' published Application No. U.S. 2006/0234331 A1), and is reproduced as follows:

> The reason why a strain having high stress response has high expression and high activity is not clear. It is however presumably related to the fact that expression of an exogenous gene is a type of stress. Besides, since high stress response can be considered to act to suppress expression of an exogenous gene and alleviate stress, the finding that a strain having high stress response has high expression and high activity according to the invention could not have been expected at all.

So as to further distinguish over the cited prior art, claim 4 has been amended to incorporate therein the recitation of claims 6 and 7. In this regard, stable expression over repeated sub-culturing is different from high activity expression. Further, even if it would have been obvious to select for high expression activity based on stress response, which Applicants dispute, claim 7 (as incorporated in claim 4) defines a strain that is separately patentable. That is, there is no connection in the prior art between stress response and stable expression.

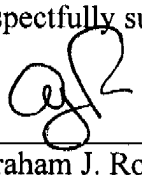
Thus, it is respectfully submitted that the amended claims are patentable over the cited prior art, and withdrawal of the foregoing rejection under 35 U.S.C. § 103(a) is respectfully requested.

Withdrawal of all rejections, rejoinder of withdrawn method claim 1 and allowance of claims 1, 4, 10-13 and 16 is earnestly solicited.

In the event that the Examiner believes that it may be helpful to advance the prosecution of this application, the Examiner is invited to contact the undersigned at the local Washington, D.C. telephone number indicated below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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